

SUPPLEMENTARY MATERIAL**Supplementary Table 1 Pharmacy costs used in the analyses**

Medication	Pack contents	Pack price (EUR)
Once-weekly semaglutide 0.5 mg	2 mg	104.03
Once-weekly semaglutide 1 mg	4 mg	104.03
Dulaglutide 0.75 mg	3 mg	92.64
Dulaglutide 1.5 mg	6 mg	90.45
Insulin glargine (Lantus Solostar)	1,500 IU	45.01
Metformin	45,000 mg	1.23
Gliclazide	1,800 mg	4.83
Needles (b-d microfine + pentip 5mm thinwall)	100 needles	16,70
SMBG test strips (Glukotest teststrip)	50 test strips	4.88
SMBG lancets (One Touch ultra soft)	10 lancets	0.94

EUR, 2017 euros; IU, international units; SMBG, self-monitoring of blood glucose.

Supplementary Table 2 Cost of treating diabetes-related complications

	Cost (EUR)	Reference
Cardiovascular complications		
Myocardial infarction year of the event	6,988	1,2,3,4,5,6,7,8,9
Myocardial infarction subsequent years	1,176	5,6,7,8,9
Angina year of the event	1,819	1,2,3,4,5,6,7,8,9,10,11,12
Angina subsequent years	358	5,6,7,8,9,10,11,12
Congestive heart failure year of the event	7,314	4,8,13,14
Congestive heart failure subsequent years	1,286	4,8,14
Stroke year of the event	23,505	2,4,9,15,16,17
Stroke subsequent years	11,625	2,4,9,15,16,17
Stroke death within 30 days	4,943	2,4,9,15,16,17
Peripheral vascular disease year of the event	4,919	4,6,8,9,18,19,20
Peripheral vascular disease subsequent years	107	8,9,18
Renal complications		
Haemodialysis year of the event	78,942	8,21
Haemodialysis subsequent years	78,942	8,21
Peritoneal dialysis year of the event	75,373	8,21
Peritoneal dialysis subsequent years	75,373	8,21
Renal transplant year of the event	33,402	8,21
Renal transplant subsequent years	4,056	8,21
Hypoglycaemic events		
Non-severe hypoglycaemic event	1	22
Severe hypoglycaemic event	486	22
Ophthalmic complications		
Laser treatment	561	21
Cataract operation year of the event	1,444	8,21,23,24
Cataract operation subsequent years	0	Assumed
Blindness	3,766	4,25,26

	Cost (EUR)	Reference
Ulcer, amputation and neuropathy complications		
Neuropathy year of the event	0	Assumed
Neuropathy subsequent years	0	Assumed
Amputation	14,610	4,21,27
Prosthesis	4,574	4,28,29
Gangrene treatment	3,195	30
Healed ulcer	201	4,31
Infected ulcer	2,454	30
Uninfected ulcer treatment	1,460	30

EUR, 2017 euros.

Supplementary Table 3 Once-weekly semaglutide 0.5 mg versus insulin glargine: Sensitivity analysis results

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Base case	+0.19	+2,152	+949	11,310	4,988
30 year time horizon	+0.16	+2,233	+1,167	13,688	7,157
0% discount rates	+0.24	+2,377	+914	9,726	3,741
HbA1c difference only	+0.08	+2,383	+1,612	31,556	21,350
Blood pressure difference only	+0.02	+2,438	+2,150	104,639	92,291
Lipid difference only	+0.01	+2,443	+2,410	277,640	273,845
BMI difference only	+0.06	+2,513	+2,482	41,741	41,223
Hypoglycaemia difference only	0.00	+2,631	+2,620	Once-weekly semaglutide equally effective but more costly	Once-weekly semaglutide equally effective but more costly
Include only significantly different treatment effects (HbA1c, systolic blood pressure, total cholesterol, LDL cholesterol and BMI)	+0.18	+2,125	+1,034	11,992	5,836
UKPDS progression for HbA1c with no changes on treatment switch	+0.18	+2,128	+1,000	11,630	5,466

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Upper 95% CI of HbA1c estimated treatment difference	+0.19	+2,050	+678	10,574	3,495
Lower 95% CI of HbA1c estimated treatment difference	+0.18	+2,300	+1,384	12,772	7,684
Upper 95% CI of BMI estimated treatment difference	+0.21	+2,150	+877	10,435	4,259
Lower 95% CI of BMI estimated treatment difference	+0.19	+2,128	+944	11,325	5,023
Treatment switching at 2 years in all arms	+0.17	+1,299	+440	7,647	2,587
Treatment switching at 5 years in all arms	+0.22	+3,443	+1,865	15,432	8,360
Treatment switching at 7.5% HbA1c threshold (including use of UKPDS progression)	+0.21	+1,910	+706	9,242	3,417
Cost of complications +10%	+0.19	+2,105	+800	11,063	4,203
Cost of complications -10%	+0.19	+2,199	+1,110	11,557	5,833
UKPDS 82 risk equations applied	+0.11	+2,158	+1,314	20,166	12,280

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Lee et al. BMI disutility applied	+0.20	+2,152	+949	10,639	4,692
Utilities converted to Dutch values	+0.20	+2,152	+949	10,931	4,821
Utilities +10%	+0.21	+2,152	+949	10,367	4,572
Utilities -10%	+0.17	+2,152	+949	12,427	5,480
Currie et al. hypoglycaemia disutilities	+0.19	+2,152	+949	11,269	4,969
Probabilistic sensitivity analysis	+0.19	+2,151	+1,295	11,453	6,894

BMI, body mass index; EUR, 2017 euros; HbA1c, glyated haemoglobin; ICER, incremental cost-effectiveness ratio; LDL, low-density lipoprotein; QALY, quality-adjusted life year;

UKPDS, United Kingdom Prospective Diabetes Study.

Supplementary Table 4 Once-weekly semaglutide 1 mg versus insulin glargine: Sensitivity analysis results

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Base case	+0.27	+2,027	+133	7,515	495
30 year time horizon	+0.25	+1,958	+159	8,002	651
0% discount rates	+0.35	+2,194	-111	6,266	Once-weekly semaglutide dominant
HbA1c difference only	+0.11	+2,187	+675	19,163	5,915
Blood pressure difference only	+0.02	+2,476	+2,211	103,595	92,490
Lipid difference only	+0.06	+2,489	+2,364	42,404	40,277
BMI difference only	+0.09	+2,626	+2,562	29,575	28,851
Hypoglycaemia difference only	0.00	+2,637	+2,668	Once-weekly semaglutide equally effective but more costly	Once-weekly semaglutide equally effective but more costly
Include only significantly different treatment effects (HbA1c, systolic blood pressure, total cholesterol, LDL cholesterol, triglycerides and BMI)	+0.29	+2,050	+167	7,000	571

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
UKPDS progression for HbA1c with no changes on treatment switch	+0.29	+1,944	-135	6,791	Once-weekly semaglutide dominant
Upper 95% CI of HbA1c estimated treatment difference	+0.30	+1,994	-118	6,554	Once-weekly semaglutide dominant
Lower 95% CI of HbA1c estimated treatment difference	+0.27	+2,077	+297	7,576	1,084
Upper 95% CI of BMI estimated treatment difference	+0.29	+2,048	+181	7,105	628
Lower 95% CI of BMI estimated treatment difference	+0.26	+2,080	+201	8,035	774
Treatment switching at 2 years in all arms	+0.24	+1,393	-296	5,698	Once-weekly semaglutide dominant
Treatment switching at 5 years in all arms	+0.37	+3,161	+923	8,631	2,519
Treatment switching at 7.5% HbA1c threshold (including use of UKPDS progression)	+0.35	+2,191	+10	6,356	30

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Cost of complications +10%	+0.27	+1,964	-101	7,281	Once-weekly semaglutide dominant
Cost of complications -10%	+0.27	+2,090	+378	7,750	1,401
UKPDS 82 risk equations applied	+0.17	+1,989	+540	11,888	3,226
Lee et al. BMI disutility applied	+0.29	+2,027	+133	6,925	456
Utilities converted to Dutch values	+0.28	+2,027	+133	7,265	478
Utilities +10%	+0.30	+2,027	+133	6,857	451
Utilities -10%	+0.24	+2,027	+133	8,297	546
Currie et al. hypoglycaemia disutilities	+0.28	+2,027	+133	7,368	485
Probabilistic sensitivity analysis	+0.28	+2,056	+570	7,239	2,007

BMI, body mass index; EUR, 2017 euros; HbA1c, glycated haemoglobin; ICER, incremental cost-effectiveness ratio; LDL, low-density lipoprotein; QALY, quality-adjusted life year;

UKPDS, United Kingdom Prospective Diabetes Study.

Supplementary Table 5 Once-weekly semaglutide 0.5 mg versus dulaglutide 0.75 mg: Sensitivity analysis results

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Base case	+0.07	+314	-446	4,671	Once-weekly semaglutide dominant
30 year time horizon	+0.08	+313	-504	3,877	Once-weekly semaglutide dominant
0% discount rates	+0.08	+367	-554	4,357	Once-weekly semaglutide dominant
HbA1c difference only	+0.04	+428	-254	10,465	Once-weekly semaglutide dominant
Blood pressure difference only	+0.01	+429	+406	41,203	39,050
Lipid difference only	-0.02	+406	+393	Once-weekly semaglutide dominated	Once-weekly semaglutide dominated
BMI difference only	+0.05	+489	+408	10,288	8,581
Hypoglycaemia difference only	0.00	+506	+526	Once-weekly semaglutide equally effective but more costly	Once-weekly semaglutide equally effective but more costly
Include only significantly different treatment effects (HbA1c and BMI)	+0.08	+377	-339	4,573	Once-weekly semaglutide dominant

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
UKPDS progression for HbA1c with no changes on treatment switch	+0.11	+355	-589	3,276	Once-weekly semaglutide dominant
Upper 95% CI of HbA1c estimated treatment difference	+0.09	+358	-616	4,104	Once-weekly semaglutide dominant
Lower 95% CI of HbA1c estimated treatment difference	+0.05	+373	-13	7,366	Once-weekly semaglutide dominant
Upper 95% CI of BMI estimated treatment difference	+0.09	+288	-467	3,239	Once-weekly semaglutide dominant
Lower 95% CI of BMI estimated treatment difference	+0.06	+287	-400	4,811	Once-weekly semaglutide dominant
Treatment switching at 2 years in all arms	+0.05	+194	-382	4,064	Once-weekly semaglutide dominant
Treatment switching at 5 years in all arms	+0.14	+371	-708	2,613	Once-weekly semaglutide dominant
Treatment switching at 7.5% HbA1c threshold (including use of UKPDS progression)	+0.11	+355	-589	3,276	Once-weekly semaglutide dominant

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Cost of complications +10%	+0.07	+303	-528	4,498	Once-weekly semaglutide dominant
Cost of complications -10%	+0.07	+326	-358	4,845	Once-weekly semaglutide dominant
UKPDS 82 risk equations applied	+0.06	+13	-704	231	Once-weekly semaglutide dominant
Lee et al. BMI disutility applied	+0.08	+314	-446	4,220	Once-weekly semaglutide dominant
Utilities converted to Dutch values	+0.07	+314	-446	4,692	Once-weekly semaglutide dominant
Utilities +10%	+0.07	+314	-446	4,434	Once-weekly semaglutide dominant
Utilities -10%	+0.06	+314	-446	5,266	Once-weekly semaglutide dominant
Currie et al. hypoglycaemia disutilities	+0.07	+314	-446	4,837	Once-weekly semaglutide dominant
Probabilistic sensitivity analysis	+0.09	+162	-404	1,717	Once-weekly semaglutide dominant

BMI, body mass index; EUR, 2017 euros; HbA1c, glycated haemoglobin; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; UKPDS, United Kingdom

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Supplementary Table 6 Once-weekly semaglutide 1 mg versus dulaglutide 1.5 mg: Sensitivity analysis results

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Base case	+0.13	+381	-455	2,861	Once-weekly semaglutide dominant
30 year time horizon	+0.12	+103	-786	870	Once-weekly semaglutide dominant
0% discount rates	+0.17	+515	-507	2,956	Once-weekly semaglutide dominant
HbA1c difference only	+0.05	+393	-258	8,304	Once-weekly semaglutide dominant
Blood pressure difference only	+0.02	+556	+430	31,577	24,446
Lipid difference only	+0.02	+631	+667	33,579	35,486
BMI difference only	+0.06	+637	+626	11,623	11,425
Hypoglycaemia difference only	0.00	+575	+602	Once-weekly Semaglutide equally effective but more costly	Once-weekly Semaglutide equally effective but more costly
Include only significantly different treatment effects (HbA1c and BMI)	+0.11	+535	-108	4,705	Once-weekly semaglutide dominant

	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
UKPDS progression for HbA1c with no changes on treatment switch	+0.15	+126	-1,083	850	Once-weekly semaglutide dominant
Upper 95% CI of HbA1c estimated treatment difference	+0.15	+298	-732	2,031	Once-weekly semaglutide dominant
Lower 95% CI of HbA1c estimated treatment difference	+0.12	+544	+22	4,470	178
Upper 95% CI of BMI estimated treatment difference	+0.15	+409	-428	2,714	Once-weekly semaglutide dominant
Lower 95% CI of BMI estimated treatment difference	+0.12	+403	-421	3,511	Once-weekly semaglutide dominant
Treatment switching at 2 years in all arms	+0.08	+159	-610	1,883	Once-weekly semaglutide dominant
Treatment switching at 5 years in all arms	+0.15	+243	-870	1,638	Once-weekly semaglutide dominant
Treatment switching at 7.5% HbA1c threshold (including use of UKPDS progression)	+0.18	+713	-449	3,953	Once-weekly semaglutide dominant

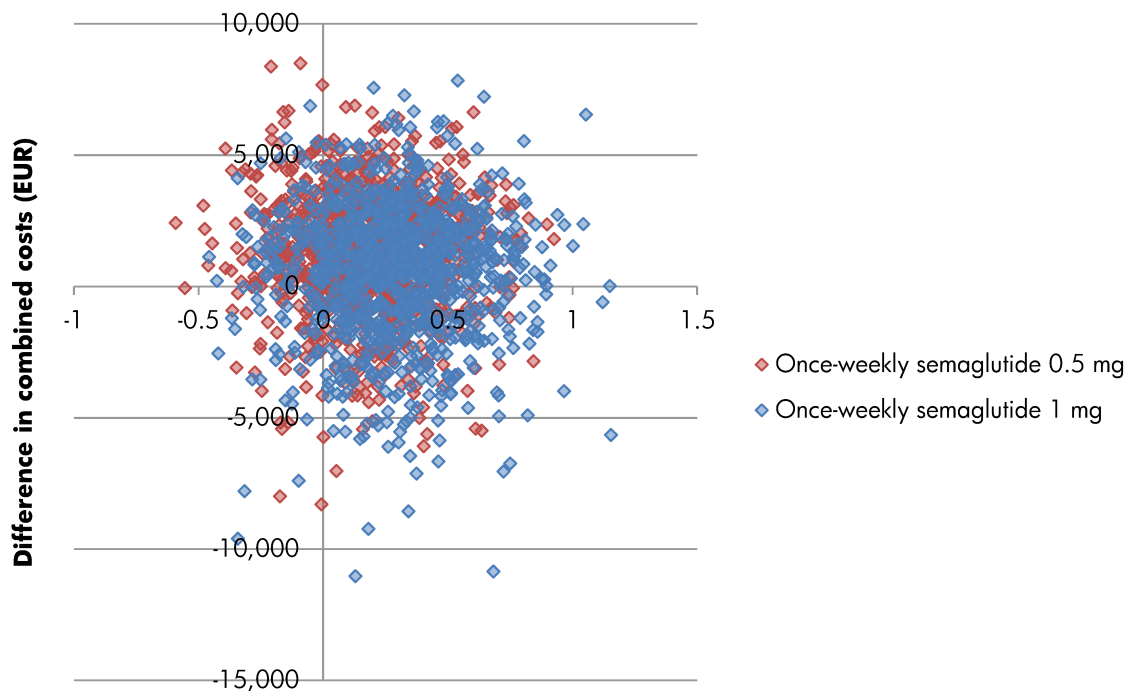
	Difference in quality-adjusted life expectancy (QALYs)	Difference in direct costs (EUR)	Difference in combined costs (EUR)	ICER based on direct costs (EUR per QALY gained)	ICER based on combined costs (EUR per QALY gained)
Cost of complications +10%	+0.13	+364	-547	2,740	Once-weekly semaglutide dominant
Cost of complications -10%	+0.13	+397	-360	2,982	Once-weekly semaglutide dominant
UKPDS 82 risk equations applied	+0.06	+332	-225	5,749	Once-weekly semaglutide dominant
Lee et al. BMI disutility applied	+0.14	+381	-455	2,672	Once-weekly semaglutide dominant
Utilities converted to Dutch values	+0.14	+381	-455	2,767	Once-weekly semaglutide dominant
Utilities +10%	+0.15	+381	-455	2,624	Once-weekly semaglutide dominant
Utilities -10%	+0.12	+381	-455	3,140	Once-weekly semaglutide dominant
Currie et al. hypoglycaemia disutilities	+0.13	+381	-455	2,855	Once-weekly semaglutide dominant
Probabilistic sensitivity analysis	+0.12	+204	-452	1,722	Once-weekly semaglutide dominant

BMI, body mass index; EUR, 2017 euros; HbA1c, glycated haemoglobin; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; UKPDS, United Kingdom

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Supplementary Figure 1 Cost-effectiveness scatterplot for once-weekly semaglutide

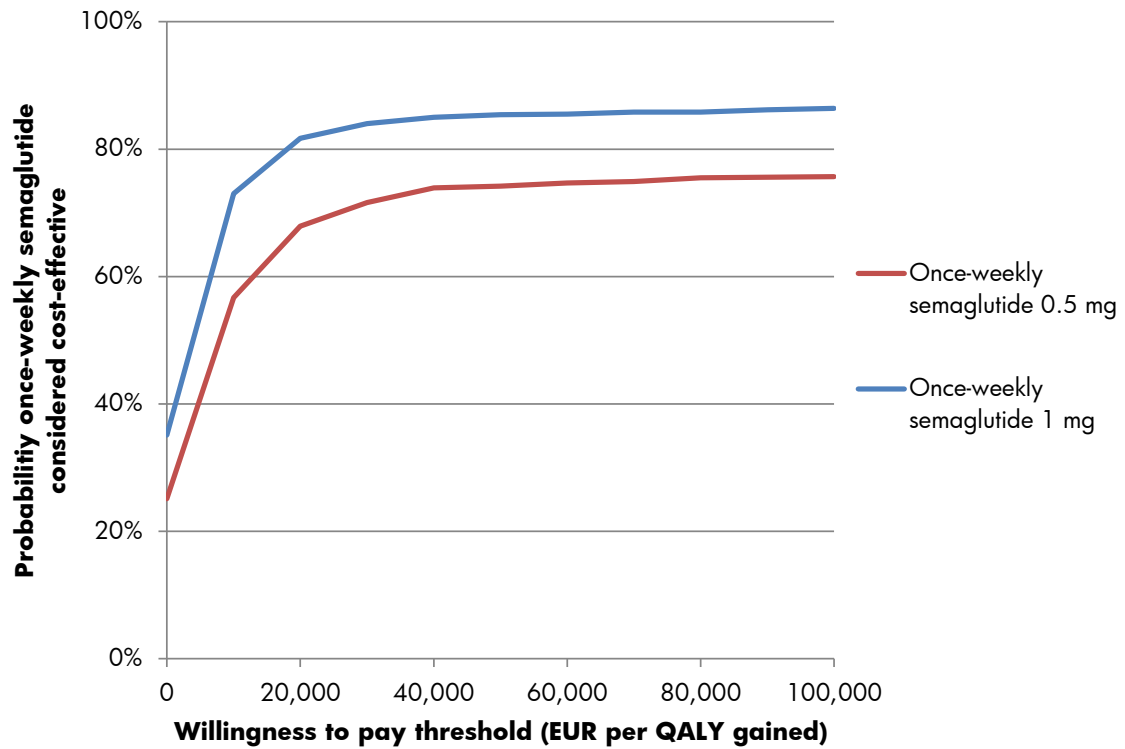
0.5 mg and 1 mg versus insulin glargine based on combined costs



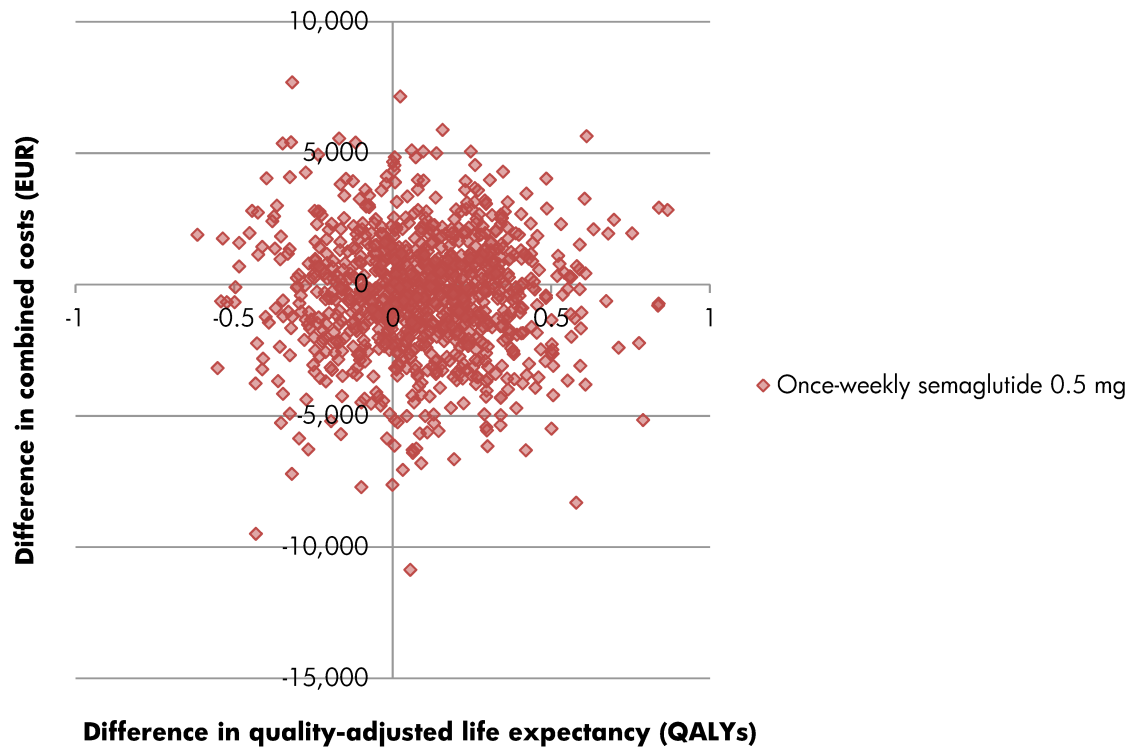
Difference in quality-adjusted life expectancy (QALYs)

EUR, 2017 euros; QALY, quality-adjusted life year. In the comparison of once-weekly semaglutide 0.5 mg with insulin glargine, 58% of points fell in the north-east quadrant (improved outcomes and increased costs), 20% in the south-east quadrant (improved outcomes and decreased costs), 5% in the south-west quadrant (poorer outcomes with decreased costs) and 17% in the north-west quadrant (poorer outcomes with increased costs). In the comparison of once-weekly semaglutide 1 mg with insulin glargine, 56% of points fell in the north-east quadrant (improved outcomes and increased costs), 31% in the south-east quadrant (improved outcomes and decreased costs), 4% in the south-west quadrant (poorer outcomes with decreased costs) and 9% in the north-west quadrant (poorer outcomes with increased costs).

Supplementary Figure 2 Cost-effectiveness acceptability curve for once-weekly semaglutide 0.5 mg and 1 mg versus insulin glargine based on combined costs

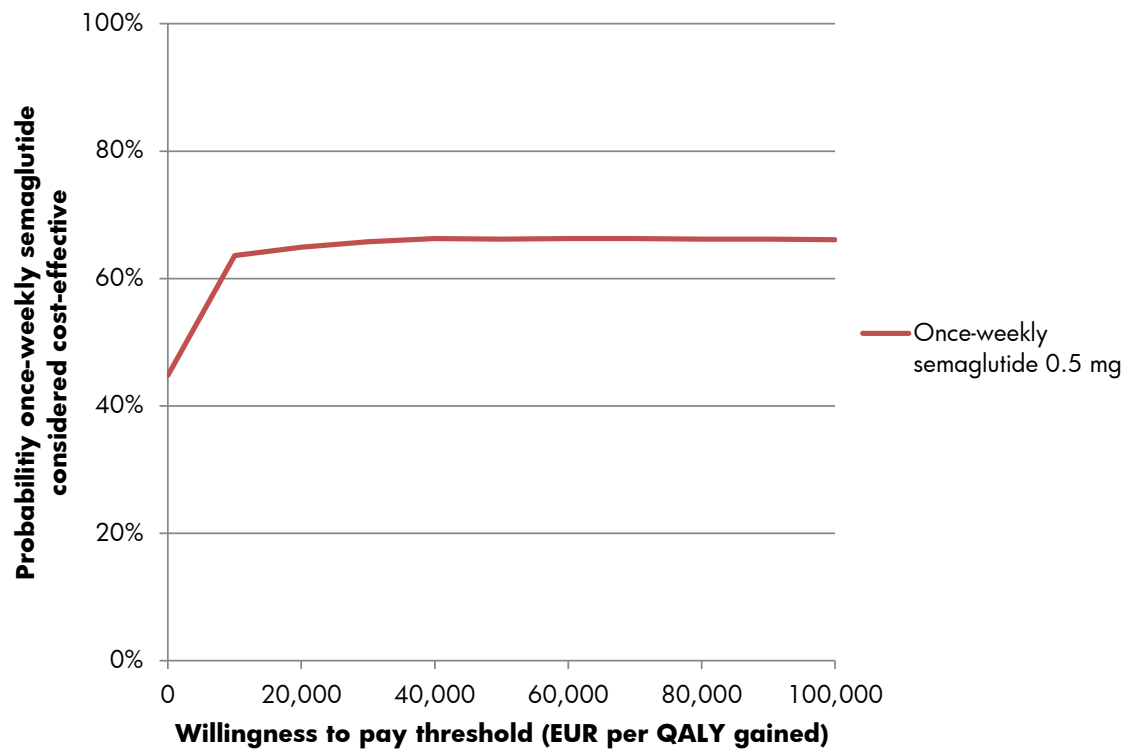


EUR, 2017 euros; QALY, quality-adjusted life year.

Supplementary Figure 3 Cost-effectiveness scatterplot for once-weekly semaglutide**0.5 mg versus dulaglutide 0.75 mg based on combined costs**

EUR, 2017 euros; QALY, quality-adjusted life year. In the comparison of once-weekly semaglutide 0.5 mg with dulaglutide 0.75 mg, 30% of points fell in the north-east quadrant (improved outcomes and increased costs), 37% in the south-east quadrant (improved outcomes and decreased costs), 19% in the south-west quadrant (poorer outcomes with decreased costs) and 14% in the north-west quadrant (poorer outcomes with increased costs).

Supplementary Figure 4 Cost-effectiveness acceptability curve for once-weekly semaglutide 0.5 mg versus dulaglutide 0.75 mg based on combined costs

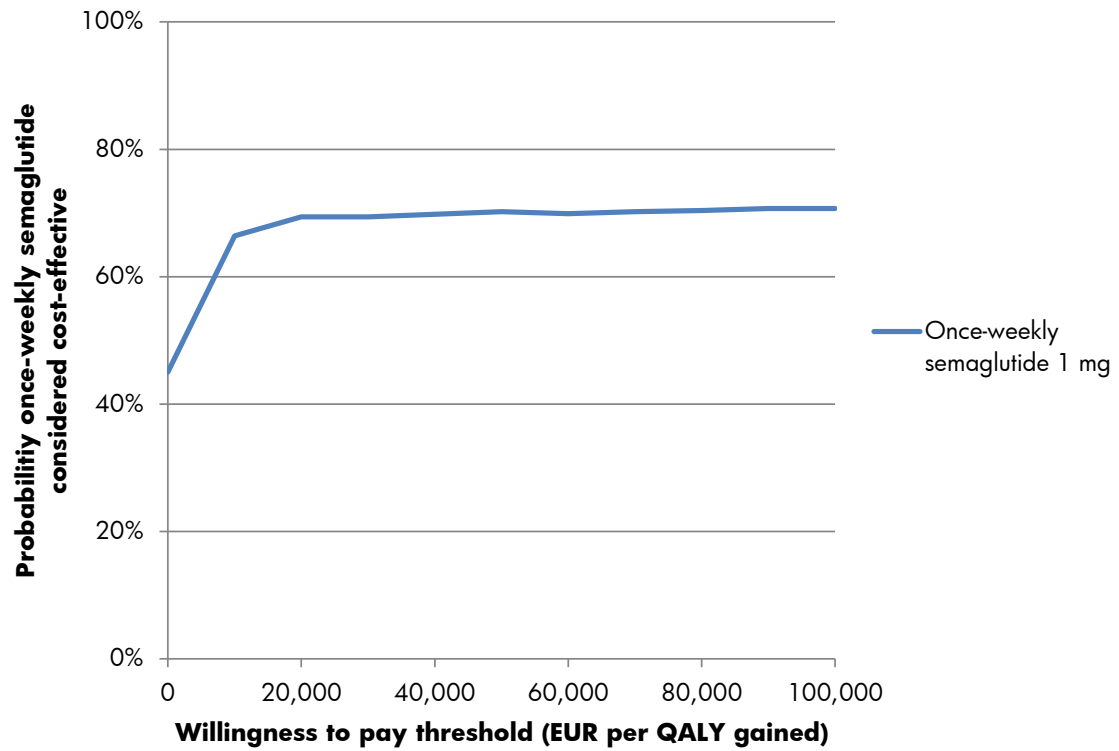


EUR, 2017 euros; QALY, quality-adjusted life year.

Supplementary Figure 5 Cost-effectiveness scatterplot for once-weekly semaglutide**1 mg versus dulaglutide 1.5 mg based on combined costs**

EUR, 2017 euros; QALY, quality-adjusted life year. In the comparison of once-weekly semaglutide 1 mg with dulaglutide 1.5 mg, 30% of points fell in the north-east quadrant (improved outcomes and increased costs), 40% in the south-east quadrant (improved outcomes and decreased costs), 17% in the south-west quadrant (poorer outcomes with decreased costs) and 13% in the north-west quadrant (poorer outcomes with increased costs).

Supplementary Figure 6 Cost-effectiveness acceptability curve for once-weekly semaglutide 1 mg versus dulaglutide 1.5 mg based on combined costs



EUR, 2017 euros; QALY, quality-adjusted life year.

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